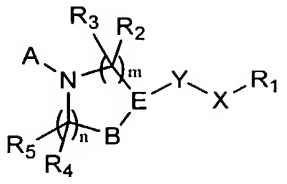
WE CLAIM

1. A compound of Formula I:



in which:

n is chosen from 0, 1 and 2; m is chosen from 1, 2 and 3;

R_1 is chosen from C_{6-10}aryl and C_{5-10}heteroaryl; wherein any aryl or heteroaryl of R_1 is optionally substituted by a radical chosen from C_{6-10}arylC_{0-4}alkyl, C_{5-6}heteroarylC_{0-4}alkyl, C_{3-8}cycloalkylC_{0-4}alkyl, C_{3-8}heterocycloalkylC_{0-4}alkyl or C_{1-10}alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R_1 can be optionally substituted by 1 to 5 radicals chosen from halo, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy; and any alkyl group of R_1 can optionally have a methylene replaced by an atom or group chosen from –S–, –S(O)–, $-S(O)_2-$, $-NR_7-$ and –O–; wherein R_7 is chosen from hydrogen and C_{1-6}alkyl;

R_2, R_3, R_4 and R_5 are independently chosen from hydrogen, halo, hydroxy, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy;

A is chosen from $-X_1C(O)OR_7$, $-X_1OP(O)(OR_7)_2$, $-X_1P(O)(OR_7)_2$, $-X_1P(O)OR_7$, $-X_1S(O)_2OR_7$, $-X_1P(O)(R_7)OR_7$ and 1*H*-tetrazol-5-yl; wherein X_1 is chosen from a bond, C_{1-3}alkylene and C_{2-3}alkenylene and R_7 is chosen from hydrogen and C_{1-6}alkyl;

B is CR_8R_9; wherein R_8 and R_9 are independently chosen from hydrogen, hydroxy, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy;

E is chosen from CR_8 or N; wherein R_8 is chosen from hydrogen, hydroxy, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy; or B is CR_9 and E is carbon and B and E are connected via a double bond;

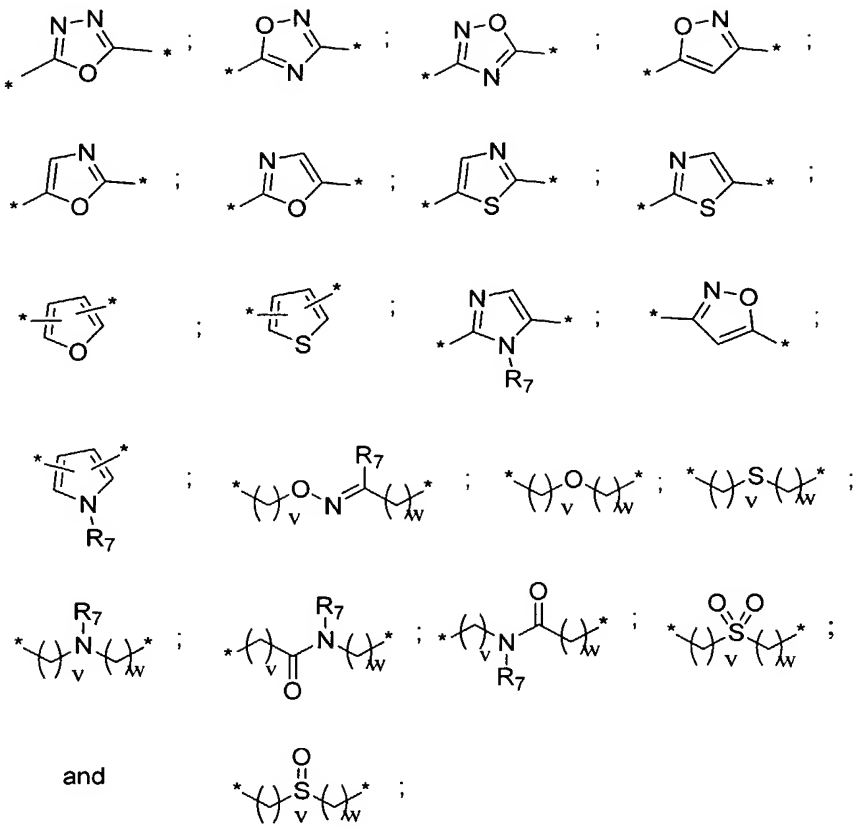
X is a bond or is chosen from $-X_1OX_2-$, $-X_1NR_7X_2-$, $-X_1C(O)NR_7X_2-$, $-X_1NR_7C(O)X_2-$, $-X_1S(O)X_2-$, $-X_1S(O)_2X_2-$, $-X_1SX_2-$, C_{4-6}heteroarylene and $-X_1ON=C(R_7)X_2-$; wherein X_1 and X_2 are independently chosen from a bond, C_{1-3}alkylene and C_{2-3}alkenylene; R_7 is chosen from hydrogen and C_{1-6}alkyl; and any heteroarylene of X is optionally substituted by a member of the group chosen from halo and C_{1-6}alkyl;

Y is chosen from C_{6-10}aryl and C_{5-10}heteroaryl, wherein any aryl or heteroaryl of Y can be optionally substituted with 1 to 3 radicals chosen from halo, hydoxy, nitro, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted C_{1-10}alkyl and halo-substituted C_{1-10}alkoxy; and the pharmaceutically acceptable salts, hydrates, solvates, isomers and prodrugs thereof.

2. The compound of claim 1 in which R_1 is chosen from phenyl, naphthyl and thiophenyl optionally substituted by C_{6-10}arylC_{0-4}alkyl, C_{5-6}heteroarylC_{0-4}alkyl, C_{3-8}cycloalkylC_{0-4}alkyl, C_{3-8}heterocycloalkylC_{0-4}alkyl or C_{1-10}alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R_1 can be optionally substituted by 1 to 5 radicals chosen from halo, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy; and any alkyl group of R_1 can optionally have a methylene replaced by an atom or group chosen from –S–, –S(O)–, $-S(O)_2-$, $-NR_7-$ and –O–; wherein R_7 is hydrogen or C_{1-6}alkyl.

3. The compound of claim 1 in which A is chosen from $-X_1C(O)OR_7$ and 1*H*-tetrazol-5-yl; wherein X_1 is chosen from a bond, C_{1-3}alkylene and C_{2-3}alkenylene and R_7 is chosen from hydrogen and C_{1-6}alkyl.

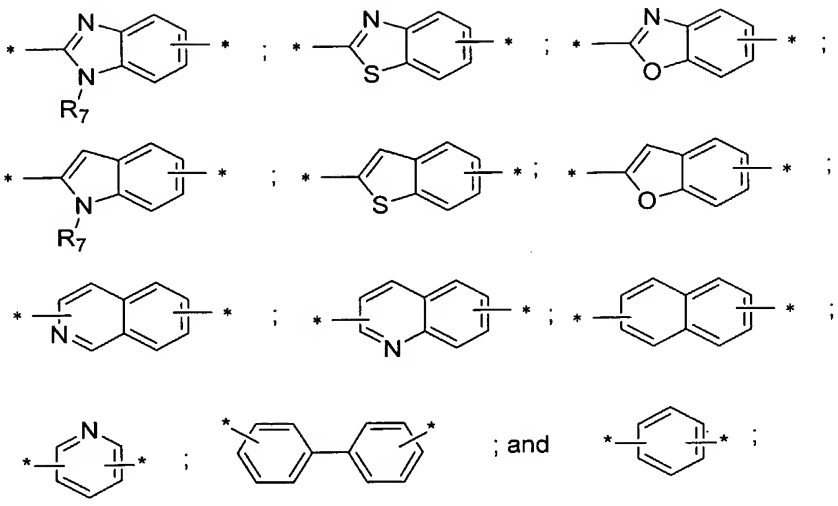
4. The compound of claim 1 in which X is chosen from:



and

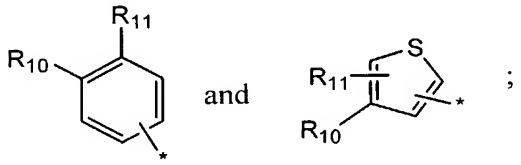
wherein the left and right asterisks of X indicate the point of attachment between R_1 and Y of Formula I, respectively; R_7 is chosen from hydrogen and C_{1-6}alkyl; v and w are independently 0, 1, 2 or 3.

5. The compound of claim 1 in which Y is chosen from:



wherein R_7 is hydrogen or C_{1-6}alkyl; and the left and right asterisks of Y indicate the point of attachment between X and E of Formula I, respectively.

6. The compound of claim 2 in which R_1 is chosen from:

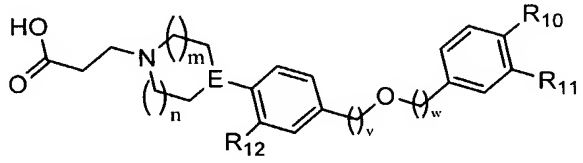


wherein the asterisk is the point of attachment of R_1 with X; R_{10} is C_{6-10}arylC_{0-4}alkyl, C_{5-6}heteroarylC_{0-4}alkyl, C_{3-8}cycloalkylC_{0-4}alkyl, C_{3-8}heterocycloalkylC_{0-4}alkyl or C_{1-10}alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R_{10} can be optionally substituted by 1 to 3 radicals chosen from halo, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy; and any alkyl group of R_{10} can optionally have a methylene replaced by an atom or group chosen from –S–, –S(O)–, –$S(O)_2$–, –NR_7– and –O–; wherein R_7 is hydrogen or C_{1-6}alkyl; and R_{11} is selected from halo, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy.

7. The compound of claim 2 selected from: 3-{4-[6-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-pyridin-3-yl]-piperazin-1-yl}-propionic acid; 3-{4-[6-(4-

Cyclohexyl-3-trifluoromethyl-phenoxymethyl)-pyridin-3-yl]-piperazin-1-yl}-propionic acid; 3-{4-[6-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-pyridazin-3-yl]-piperazin-1-yl}-propionic acid; 3-{4-[2-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-pyrimidin-5-yl]-piperazin-1-yl}-propionic acid; 3-{4-Hydroxy-4-[2-(2-trifluoromethyl-biphenyl-4-yl)-benzo[b]thiophen-5-yl]-piperidin-1-yl}-propionic acid; 3-{4-[2-(2-Trifluoromethyl-biphenyl-4-yl)-benzo[b]thiophen-5-yl]-3,6-dihydro-2H-pyridin-1-yl}-propionic acid; 3-(3-{4-[3-(2-Trifluoromethyl-biphenyl-4-yl)-[1,2,4]oxadiazol-5-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(3-{3-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(3-{3-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(3-{4-[3-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(4-{4-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-piperidin-1-yl)-propionic acid; 3-(3-{4-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(3-{4-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(4-{4-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-piperidin-1-yl)-propionic acid; 3-(3-{4-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-azetidin-1-yl)-propionic acid; 3-(3-{4-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-azetidin-1-yl)-propionic acid; 3-(4-{4-[5-(3-Trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-piperidin-1-yl)-propionic acid; 3-{4-[6-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-pyridin-3-yl]-piperazin-1-yl}-propionic acid; and 3-{4-[4-(2-Trifluoromethyl-biphenyl-4-ylsulfanylmethyl)-phenyl]-piperidin-1-yl}-propionic acid.

8. The compound of claim 2 of Formula Ia:



(Ia)

in which:

E is selected from N and CH;

m and n are independently selected from 0 and 1;

v and w are independently selected from 0 and 1;

R_{10} is selected from cyclohexyl, piperidinyl, tetrahydro-thiopyran-4-yl, phenyl, phenoxy and phenylsulfanyl; wherein any cyclohexyl, piperidinyl, tetrahydro-thiopyran-4-yl, phenyl, phenoxy and phenylsulfanyl of R_{10} can be optionally substituted by 1 to 3 radicals independently selected from methyl and isopropyl;

R_{11} is selected from methyl, trifluoromethyl and ethyl; and

R_{12} is selected from hydrogen, ethyl and methoxy.

9. The compound of claim 8 selected from: 3-{4-[4-(4-Cyclohexyl-3-methyl-phenoxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Piperidin-1-yl-3-trifluoromethyl-phenoxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-(4-{4-[3-Methyl-4-(tetrahydro-thiopyran-4-yl)-phenoxymethyl]-phenyl}-piperidin-1-yl)-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-2-ethyl-phenyl]-piperazin-1-yl}-propionic acid; 3-{4-[4-(2-Methyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-phenoxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(3'-Methyl-2-trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{3-[4-(4-Cyclohexyl-3-trifluoromethyl-phenoxymethyl)-phenyl]-pyrrolidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-ethyl-phenoxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-pyrrolidin-1-yl}-propionic acid; 3-(4-{4-[4-(3,6-Dihydro-2H-thiopyran-4-yl)-3-trifluoromethyl-phenoxymethyl]-phenyl}-piperidin-1-yl)-propionic acid; 3-{3-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-phenyl]-azetidin-1-yl}-propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-azetidin-1-yl}-propionic acid; 3-{4-[2-Ethyl-4-(2-trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{3-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-phenyl]-pyrrolidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-

benzyloxy)-2-ethyl-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4'-Methyl-2-trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Phenoxy-3-trifluoromethyl-phenoxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-phenoxymethyl)-2-methoxy-phenyl]-piperazin-1-yl}-propionic acid; 3-{4-[4-(2-Trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidin-1-yl}-propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-pyrrolidin-1-yl}-propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-azetidin-1-yl}-propionic acid; 3-{4-[4-(4-Isobutyl-3-trifluoromethyl-benzyloxy)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Phenylsulfanyl-3-trifluoromethyl-phenoxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 1-(1H-Tetrazol-5-ylmethyl)-4-[4-(2-trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidine; 1-[2-(1H-Tetrazol-5-yl)-ethyl]-4-[4-(2-trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidine; 3-{4-[4-(2,4'-Dimethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(2,4'-Dimethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(2-Ethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(2-Ethyl-3'-methyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; (2-{4-[4-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-ethyl)-phosphonic acid; 2-{4-[4-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-ethanesulfonic acid; and Phosphoric acid mono-(2-{4-[4-(2-trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-ethyl) ester.

10. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with a pharmaceutically acceptable excipient.

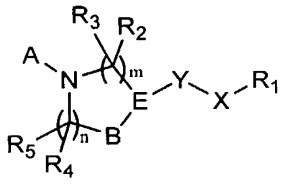
11. A method for treating a disease in an animal in which alteration of EDG/S1P receptor mediated signal transduction can prevent, inhibit or ameliorate the pathology and/or symptomology of the disease, which method comprises administering to the animal a therapeutically effective amount of a compound of Claim 1.

12. A method for preventing or treating disorders or diseases mediated by lymphocytes, for preventing or treating acute or chronic transplant rejection or T-cell

mediated inflammatory or autoimmune diseases, for inhibiting or controlling deregulated angiogenesis, or for preventing or treating diseases mediated by a neo-angiogenesis process or associated with deregulated angiogenesis in a subject comprising administering to the subject in need thereof an effective amount of a compound of claims1, or a pharmaceutically acceptable salt thereof.

13. The use of a compound of claim 1 in the manufacture of a medicament for treating a disease in an animal in which alteration of EDG/S1P receptor mediated signal transduction contributes to the pathology and/or symptomology of the disease.

14. A process for preparing a compound of Formula I:



in which:

n is chosen from 0, 1 and 2; m is chosen from 1, 2 and 3;

R_1 is chosen from C_{6-10}aryl and C_{5-10}heteroaryl; wherein any aryl or heteroaryl of R_1 is optionally substituted by a radical chosen from C_{6-10}arylC_{0-4}alkyl, C_{5-6}heteroarylC_{0-4}alkyl, C_{3-8}cycloalkylC_{0-4}alkyl, C_{3-8}heterocycloalkylC_{0-4}alkyl or C_{1-10}alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R_1 can be optionally substituted by 1 to 5 radicals chosen from halo, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy; and any alkyl group of R_1 can optionally have a methylene replaced by an atom or group chosen from –S–, –S(O)–, –$S(O)_2$–, –NR_7– and –O–; wherein R_7 is chosen from hydrogen and C_{1-6}alkyl;

R_2, R_3, R_4 and R_5 are independently chosen from hydrogen, halo, hydroxy, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy;

A is chosen from –$X_1C(O)OR_7$, –$X_1OP(O)(OR_7)_2$, –$X_1P(O)(OR_7)_2$, –$X_1P(O)OR_7$, –$X_1S(O)_2OR_7$, –$X_1P(O)(R_7)OR_7$ and 1*H*-tetrazol-5-yl; wherein X_1 is chosen from a bond, C_{1-3}alkylene and C_{2-3}alkenylene and R_7 is chosen from hydrogen and C_{1-6}alkyl;

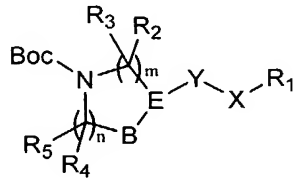
B is CR_8R_9; wherein R_8 and R_9 are independently chosen from hydrogen, hydroxy, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy;

E is chosen from CR_8 or N; wherein R_8 is chosen from hydrogen, hydroxy, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted-C_{1-10}alkyl and halo-substituted-C_{1-10}alkoxy; or B is CR_9 and E is carbon and B and E are connected via a double bond;

X is a bond or is chosen from $-X_1OX_2-$, $-X_1NR_7X_2-$, $-X_1C(O)NR_7X_2-$, $-X_1NR_7C(O)X_2-$, $-X_1S(O)X_2-$, $-X_1S(O)_2X_2-$, $-X_1SX_2-$, C_{4-6}heteroarylene and $-X_1ON=C(R_7)X_2-$; wherein X_1 and X_2 are independently chosen from a bond, C_{1-3}alkylene and C_{2-3}alkenylene; R_7 is chosen from hydrogen and C_{1-6}alkyl; and any heteroarylene of X is optionally substituted by a member of the group chosen from halo and C_{1-6}alkyl;

Y is chosen from C_{6-10}aryl and C_{5-10}heteroaryl, wherein any aryl or heteroaryl of Y can be optionally substituted with 1 to 3 radicals chosen from halo, hydoxy, nitro, C_{1-10}alkyl, C_{1-10}alkoxy, halo-substituted C_{1-10}alkyl and halo-substituted C_{1-10}alkoxy; which process comprises:

(a) reacting a compound of formula 2:



(2)

with either *t*-butyl acrylate, acylonitrile/NaN_3 or bromoacetonitrile/NaN_3; wherein B, E, Y, X, R_1 R_2, R_3, R_4 and R_5 are as described above; and

(b) optionally converting a compound of the invention into a pharmaceutically acceptable salt;

(c) optionally converting a salt form of a compound of the invention to a non-salt form;

(d) optionally converting an unoxidized form of a compound of the invention into a pharmaceutically acceptable N-oxide;

(e) optionally converting an N-oxide form of a compound of the invention to its unoxidized form;

(f) optionally resolving an individual isomer of a compound of the invention from a mixture of isomers;

(g) optionally converting a non-derivatized compound of the invention into a pharmaceutically acceptable prodrug derivative; and

(h) optionally converting a prodrug derivative of a compound of the invention to its non-derivatized form.